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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,947	11/10/2000	Brynmor Watkins	MTP-024	3918

21323 7590 09/25/2003

TESTA, HURWITZ & THIBEAULT, LLP
HIGH STREET TOWER
125 HIGH STREET
BOSTON, MA 02110

EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	16

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/709,947	WATKINS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-20 and 41-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-20 and 41-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7&15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in Paper No. 12 filed September 26, 2002 is acknowledged. The traversal is on the ground(s) that the search and examination of both sets of claims included in Groups II and III can be made without serious burden. This argument has been found persuasive. Accordingly as set forth below claims 9-20 and 41-55 from Groups II and III will be examined as one claimed invention.

Furthermore, Applicants traverses the election of one polypeptide sequence for the use in the elected method claims. "Applicants note that SEQ ID NO: 1-4 are...subsequences of SEQ ID NO: 5". This is not found persuasive because while SEQ ID NO: 1-4 may be fragments of SEQ ID NO: 5 each would require a different and distinct antibodies for their individual detection. SEQ ID NO: 1-4 do not share sequence homology. SEQ ID NO: 1 is a thirteen amino acid peptide contained with the 272 amino acid polypeptide of SEQ ID NO: 5. A separate and distinct search would be warranted for SEQ ID NO: 5. Clearly different searches and issues are involved in the examination of each sequence. For these reasons the remainder of the restriction requirement is deemed to be proper and is adhered to.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 9-20 and 41-55 are pending.

Claims 9, 15 and 41 have been amended.

Claims 1-8, 21-40 and 56-62 have been cancelled.

Claims 9-20 and 41-55 are examine d on the merits.

Information Disclosure Statement

3. The information disclosure statement filed March 18, 2003 as Paper number 15 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein as documents AD-AK, BD-BJ and CCE-CCCK has not been considered. In addition the document referenced as CP did not accompany the IDS filed January 30, 2002. Accordingly, the listed documents have not been considered and Applicants are invited to supply them.

Claim Objections

4. Claims 48-55 are objected to because of the following informality: it references non-elected SEQ ID numbers which are not examined. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 9-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9 and 15 are broadly drawn to methods of diagnosing cancer comprising the detection of a cancer-associated protein of about 28 kD. The protein is identified by its molecular weight and ability to bind a binding moiety. The specification teaches a 28.3 kD breast cancer protein, see page 40. The specification does not teach a protein identified by SEQ ID number that is the 28.3 kD breast protein, nor does it teach the plethora of proteins encompassed by the broad recitation "cancer-associated protein of about 28kD" capable of detecting any cancer as broadly set forth in claims 9 and 15-20. Applicants' specification supports the a method of diagnosing breast cancer in an individual utilizing the disclosed 28.3 kD breast protein. Applicants are not in possession of any and all cancer-associated proteins of 28 kD, which have not been defined by functional or structural characteristics and may or may not be able to diagnose any and all cancers encompassed by the broad claims.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of the 28 kD breast protein, the skilled artisan cannot envision the detailed structure or function of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptides and molecules germane to the methodology itself are required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a

representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus.

At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed Applicants only had possession of one 28.3 kD breast cancer protein and not any other polypeptides with molecular weights of about 28 kD that may or may not act in the manner suggested by the specification. The specification does not evidence the possession of all breast cancer associated or cancer-associated molecules in a method of broadly diagnosing cancer. There is insufficient support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 9-20, 41, 42 and 48-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 9, 15, 41 and 48 are vague and indefinite in the recitation " cancer-associated protein". It is not clear what properties or activities should define a protein as cancer-associated. Accordingly, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 9-11 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. (Cancer Research 43(9): 4297-4301, 1983). Adams discloses the detection of 24 kDa estrogen-regulated protein it found in human breast cancers, which the Examiner regards as a cancer-associated protein, see abstract and page 4297, column 2, second full paragraph. This 24 kDa protein is about 28kD and inherently would bind in the presence of 50nM sodium phosphate, pH 7.0, to an anion exchange resin comprising quaternary ammonium groups and elute from the said resin in the presence of 50mM sodium chloride in 50mM sodium phosphate, pH 7.0. The disclosed protein was detected in human breast tumor biopsies with a monoclonal antibody binding moiety, page 4299, Specific Detection...section.

11. Claims 9-20, 41-47 and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number 2002/0081659 (March 12, 1999). U.S. Patent Application Publication #2002/0081659 discloses sequence 687, a protein comprising SEQ ID NO: 1, see attached database sheet. Sequence 687 contains 272 amino acid residues, which is approximately 29-34 kD and within the range of about 28 kD as set forth in the claims. It is reasonable to conclude that this disclosed polypeptide would bind in the presence of 50nM sodium phosphate, pH 7.0, to an anion exchange resin comprising quaternary ammonium groups and elute from the said resin in the presence of 50mM sodium chloride in 50mM sodium phosphate, pH 7.0.

The patent application discloses diagnostic methods including antibodies that bind the disclosed polypeptide fragment within sequence 687, as well as the sequence itself, see sections 0012, 0211, 0214 and 0267-0270. The detection methods include assaying for the expression of the polypeptide in cells or body fluid in order to assess for breast cancer, see sections 0268 and 0545. The diagnostic assay for diagnosing the breast cancer disorder comprises the assaying the expression of the polypeptide of interest in cells, body fluid or serum of an individual using one or more antibodies and the expression level is compared to the standard expression level is indicative of the disorder and furthermore indicative of a comparative reference sample, see sections 0268, 0280 and 0313.

The patent application provides kits that can be used in the disclosed method, see sections 0276-0283. The kit may comprises a isolated polypeptide comprising an

epitope, which is specifically immunoreactive with an antibody (i.e. monoclonal, polyclonal and labeled) included in the kit, see sections 0162, 0271 and 0277.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 9-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (Cancer Research 43(9): 4297-4301, 1983), and further in view of U.S. Patent Application Publication number 2002/0081659 (March 12, 1999). The teachings of Adams have been presented in the 102(b) rejection. Adams does not teach that the sample isolated from the individual comprises a body fluid, such as lymph or serum. Adams does not teach that the binding moiety is a polyclonal antibody or labeled with a detectable moiety.

U.S. Patent Application Publication number 2002/0081659 teaches the production and use of several types of antibodies in the diagnosis of breast cancer from a sample comprising serum, see sections , 0161, 0267, 0280, 0365, 0543 and 0545. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to utilize antibodies, such as a labeled antibody in order to enhance detection of the antigen of interest. It also would have been *prima facie* obvious to one

of ordinary skill in the art at the time of the claimed invention to assay different biological fluids from the individual in order to correlate analyses from different samples for a definitive diagnosis of breast. One of ordinary skill in the art would have been motivated by the teachings of both, Adams and the patent application to integrate the different antibodies and varied biological samples for obtain information germane to the diagnosis of breast cancer.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
23 September 2003